IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

CYDEX PHARMACEUTICALS, INC.,	)	
	)	
Plaintiffs,	)	
	)	
v.	)	C. A. No. _____
	)	
TEVA PHARMACEUTICALS USA, INC., TEVA PHARMACEUTICAL INDUSTRIES LTD., and ACTAVIS, LLC,	)	
	)	
Defendants.	)	

COMPLAINT

Plaintiff CyDex Pharmaceuticals, Inc. ("CyDex"), by its undersigned attorneys, brings this action against Defendants Teva Pharmaceuticals USA, Inc. ("Teva USA"), Teva Pharmaceutical Industries Ltd. ("Teva Ltd."), and Actavis LLC ("Actavis") (collectively, "Teva" or "Defendants"), and hereby alleges as follows:

NATURE OF THE ACTION

1. This is an action for patent infringement under the patent laws of the United States arising from the filing of Abbreviated New Drug Application No. 209323 (the "Actavis ANDA") with the United States Food and Drug Administration ("FDA") seeking approval to market a generic version of EVOMELA® (Captisol®-enabled Melphalan HCl) for Injection.

THE PARTIES

2. Plaintiff CyDex Pharmaceuticals, Inc. is a Delaware corporation with its principal place of business at 3911 Sorrento Valley Boulevard, Suite 110, San Diego, CA 92121.

3. CyDex is informed and believes, and thereon alleges, that Defendant Teva Pharmaceuticals USA, Inc. ("Teva USA") is a Delaware corporation with its principal place of business at 1090 Horsham Road, North Wales, PA 19454.

4. CyDex is informed and believes, and thereon alleges, that Teva Pharmaceutical Industries Ltd. ("Teva Ltd.") is an Israeli company with its principal place of business at 5 Basel Street, P.O. Box 3190, Petah Tikva, 49131, Israel.

5. CyDex is informed and believes, and thereon alleges, that Defendant Actavis LLC ("Actavis") is a Delaware company with its principal place of business at 400 Interpace Pkwy, Morris Corporate Center III, Parsippany, NJ 07054.

6. CyDex is informed and believes, and thereon alleges, that Defendants participated and collaborated in the research and development, and the preparation and filing, of the Actavis ANDA for Melphalan hydrochloride for injection (the "Actavis ANDA Product"), continue to participate and collaborate in seeking FDA approval of that application, and intend to participate and collaborate in the commercial manufacture, marketing, offer for sale, and sale of the Actavis ANDA Product throughout the United States, including in the State of Delaware, in the event the FDA approves the Actavis ANDA.

JURISDICTION AND VENUE

7. This Court has jurisdiction over the subject matter of this action under 28 U.S.C. §§ 1331, 1338(a), 2201 and 2202.

8. This Court has personal jurisdiction over Teva USA at least because, CyDex is informed and believes, and thereon alleges, that Teva USA is a Delaware corporation.

9. This Court has personal jurisdiction over each of Teva USA, Teva Ltd., and Actavis, at least by virtue of their presence in Delaware, having conducted business in Delaware, having availed themselves of the rights and benefits of Delaware law such that they should reasonably anticipate being haled into court in this judicial district, and having engaged in systematic and continuous contacts with the State of Delaware through the marketing and sales

of generic drugs within this judicial district, through the receipt of revenue from the sales and marketing of generic drug products, including Teva products, within this judicial district, and through their intent to market and sell the Actavis ANDA Product, if approved, in this judicial district and to residents of this judicial district.

10. This Court also has personal jurisdiction over Teva USA and Teva Ltd. because they have previously submitted to the jurisdiction of this Court, and have availed themselves of the legal protections of the State of Delaware by having filed suit in this jurisdiction. *See, e.g.*, *Teva Pharm. USA, Inc., Teva Pharmaceutical Industries Ltd., et al. v. Amneal Pharm. LLC, et al.,* Civil Action No. 17-992, D.I. 1 (D. Del. July 20, 2017); *Teva Pharm. USA, Inc., Teva Pharmaceutical Industries Ltd., et al. v. Dr. Reddy's Labs., Ltd., et al.*, Civil Action No. 17-693, D.I. 1 (D. Del. June 7, 2017); *Teva Pharm. USA, Inc., Teva Pharmaceutical Industries Ltd., et al. v. Sandoz Inc., et al.*, Civil Action No. 17-597, D.I. 1 (D. Del. May 24, 2017); *Teva Pharm. USA, Inc., Teva Pharmaceutical Industries Ltd., et al. v. Synthon Pharm., Inc., et al.*, Civil Action No. 17-390, D.I. 1 (D. Del. April 7, 2017); *Teva Pharm. USA, Inc., Teva Pharmaceutical Industries Ltd., et al. v. Mylan Pharm. Inc., et al.*, Civil Action No. 17-249, D.I. 1 (D. Del. March 10, 2017).

11. This Court has personal jurisdiction over Actavis at least because, CyDex is informed and believes, and thereon alleges, that Actavis is a Delaware company.

12. This Court also has personal jurisdiction over Actavis by virtue of the fact that Actavis previously submitted to the jurisdiction of this Court and availed itself of this Court by consenting to this Court's jurisdiction and asserting counterclaims in civil actions initiated in this jurisdiction including, but not limited to, e.g., *Astellas Pharma Inc., et al. v. Actavis Elizabeth LLC, Actavis LLC, et al.*, Civil Action No. 16-905, D.I. 11 (D. Del. Oct. 31, 2016); *Millennium*

Pharmaceuticals, Inc. v. Actavis LLC, Civil Action No. 16-223, D.I. 7 (D. Del. Apr. 25, 2016); *Cephalon, Inc. v. Dr. Reddy's Labs., Ltd., Actavis LLC, et al.*, Civil Action No. 15-179, D.I. 1 (D. Del. March 17, 2015).

13. Alternatively, this Court has personal jurisdiction over Teva Ltd. under Fed. R. Civ. P. 4(k)(2).

14. Venue is proper in this judicial district under 28 U.S.C. §§ 1391(b) and (c) and § 1400(b).

THE PATENTS-IN-SUIT

15. On April 2, 2013, the United States Patent and Trademark Office ("USPTO") duly and lawfully issued United States Patent No. 8,410,077 ("the '077 patent"), entitled "Sulfoalkyl Ether Cyclodextrin Compositions." A true and correct copy of the '077 patent is attached hereto as Exhibit A.

16. On December 1, 2015, the USPTO duly and lawfully issued United States Patent No. 9,200,088 ("the '088 patent"), entitled "Sulfoalkyl Ether Cyclodextrin Compositions." A true and correct copy of the '088 patent is attached hereto as Exhibit B.

17. On November 15, 2016, the USPTO duly and lawfully issued United States Patent No. 9,493,582 ("the '582 patent"), entitled "Alkylated Cyclodextrin Compositions and Processes for Preparing and Using the Same." A true and correct copy of the '582 patent is attached hereto as Exhibit C.

18. CyDex Pharmaceuticals is the owner of all right, title, and interest in the '077 patent, the '088 patent, and the '582 patent (collectively, "the patents-in-suit").

19. U.S. Patent Application No. 14/229,523 ("the '523 application"), entitled "Injectable Nitrogen Mustard Compositions Comprising a Cyclodextrin Derivative and Methods

of Making and Using the Same," was filed on March 28, 2014, and published on July 31, 2014 as U.S. Patent Publication No. 2014/0213650 ("the '650 publication"). A true and correct copy of the '650 publication is attached hereto as Exhibit D.

20. U.S. Patent Application No. 14/108,169 ("the '169 application"), entitled "Injectable Melphalan Compositions Comprising a Cyclodextrin Derivative and Methods of Making and Using the Same," was filed on December 16, 2013, and published on August 7, 2014 as U.S. Patent Publication No. 2014/0221488 ("the '488 publication"). A true and correct copy of the '488 publication is attached hereto as Exhibit E.

EVOMELA®

21. Pursuant to 21 U.S.C. § 355(b)(1), and attendant FDA regulations, the patents-in-suit are listed in the FDA publication entitled Approved Drug Products and Therapeutic Equivalence Evaluations ("the Orange Book") in connection with FDA-approved New Drug Application ("NDA") No. 207155 as covering EVOMELA® (Captisol®-enabled Melphalan HCl) for Injection; 50mg (free base)/vial.

22. Cydex is informed and believes, and thereon alleges, that patents that issue from the '523 application or the '169 application may cover EVOMELA® (Captisol®-enabled Melphalan HCl) for Injection; 50mg (free base)/vial, and may be listed in the Orange Book in connection with NDA No. 207155.

THE ACTAVIS ANDA

23. On November 9, 2017, CyDex received a letter from Teva USA, dated November 8, 2017, regarding "Notification of Certification for U.S. Patent Nos. 8,410,077; 9,200,088; and 9,493,582 Pursuant to § 505(j)(2)(B)(iv) of the Federal Food, Drug, and Cosmetic Act" ("Teva's Purported Notice Letter"). Teva's Purported Notice Letter states that Teva USA had submitted

an ANDA to the FDA under 21 U.S.C. § 355(j)(1) and (2)(A), seeking FDA approval to manufacture, offer to sell, and sell a generic version of EVOMELA®.

24. The Actavis ANDA states that it was filed by Actavis.

25. Federal law requires that "[a]n ***applicant*** that makes a certification described in paragraph (2)(A)(iv) shall give notice as required under this paragraph" and that "[a]n ***applicant*** required under this paragraph to give notice shall give notice" to each patent owner and the NDA holder. 21 U.S.C. § 355(b)(3)(B) & (C) (emphases added).

26. Teva's Purported Notice Letter does not mention Actavis.

27. Teva's Purported Notice Letter does not meet the requirements of Section 355(b).

28. CyDex is informed and believes, and thereon alleges, that the Actavis ANDA was submitted to the FDA for approval to market a generic version of EVOMELA® prior to the expiration of the patents-in-suit.

29. CyDex is informed and believes, and thereon alleges, that upon FDA approval of the Actavis ANDA, Defendants will market and distribute the Actavis ANDA Product to resellers, pharmacies, hospitals and other clinics, health care professionals, and end users of the Actavis ANDA Product.

30. CyDex is informed and believes, and thereon alleges, that the Actavis ANDA refers to and relies upon the EVOMELA® NDA and contains data that, according to Actavis, demonstrate the required bioavailability and/or bioequivalence of the Actavis ANDA Product and EVOMELA®.

31. Cydex is informed and believes, and thereon alleges, that Defendants will amend the Actavis ANDA to include a certification regarding any patents that issue from the '523 application or the '169 application to the extent that such patents are listed in the Orange

Book in connection with NDA No. 207155. Cydex reserves the right to seek leave to add any such patents to this lawsuit.

COUNT I FOR INFRINGEMENT OF U.S. PATENT NO. 8,410,077

32. CyDex realleges and incorporates by reference the allegations of paragraphs 1-31 of this Complaint as if fully set forth herein.

33. Defendants infringed the ’077 patent, pursuant to 35 U.S.C. § 271(e)(2)(A), by submitting the Actavis ANDA, which seeks approval from the FDA to engage in the commercial manufacture, use, offer to sell, sale or importation of the Actavis ANDA Product prior to the expiration of the ’077 patent.

34. Defendants’ commercial manufacture, use, offer to sell, or sale of the Actavis ANDA Product within the United States, or importation of the Actavis ANDA Product into the United States, during the term of the ’077 patent also would infringe the ’077 patent under 35 U.S.C. § 271(a), (b), (c), (f) and/or (g).

35. Defendants’ commercial manufacture, use, offer to sell, or sale of the Actavis ANDA Product within the United States, or importation of the Actavis ANDA Product into the United States, during the term of the ’077 patent, would infringe at least Claim 1 of the ’077 patent because, CyDex is informed and believes, and thereon alleges, that the Actavis ANDA Product contains a sulfoalkyl ether cyclodextrin (SAE-CD) composition comprising a sulfoalkyl ether cyclodextrin having an average degree of substitution of 4.5 to 7.5 and less than 100 ppm of a phosphate, wherein the SAE-CD composition has an absorption of less than 0.5 A.U. due to a drug-degrading agent, as determined by UV/vis spectrophotometry at a wavelength of 245 nm to 270 nm for an aqueous solution containing 300 mg of the SAE-CD composition per mL of solution in a cell having a 1 cm path length.

36. Teva's Purported Notice Letter does not identify any non-infringement argument based on a contention that any limitation of any claim of the '077 patent is not satisfied by the Actavis ANDA Product.

37. Upon approval of the Actavis ANDA, and the commercial marketing of the Actavis ANDA Product, Defendants would actively induce and/or contribute to infringement of the '077 patent.

38. CyDex is informed and believes, and thereon alleges, that, at least in light of the prescribing instructions Defendants propose to provide in connection with the Actavis ANDA Product, Defendants will induce health care professionals, resellers, pharmacies, and end users of the Actavis ANDA Product to directly infringe one or more claims of the '077 patent. CyDex is informed and believes, and thereon alleges, that Defendants will encourage acts of direct infringement with knowledge of the '077 patent and knowledge that they are encouraging infringement.

39. CyDex is informed and believes, and thereon alleges, that Defendants had actual and constructive knowledge of the '077 patent prior to filing the Actavis ANDA, and were aware that the filing of the Actavis ANDA with the request for FDA approval before the expiration of the '077 patent would constitute an act of infringement of the '077 patent.

40. Defendants have no reasonable basis for asserting that the commercial manufacture, use, sale, offer for sale, and/or importation of the Actavis ANDA Product will not contribute to the infringement and/or induce the infringement of the '077 patent.

COUNT II FOR INFRINGEMENT OF U.S. PATENT NO. 9,200,088

41. CyDex realleges and incorporates by reference the allegations of paragraphs 1-40 of this Complaint as if fully set forth herein.

42. Defendants infringed the ’088 patent, pursuant to 35 U.S.C. § 271(e)(2)(A), by submitting the Actavis ANDA, which seeks approval from the FDA to engage in the commercial manufacture, use, offer to sell, sale or importation of the Actavis ANDA Product prior to the expiration of the ’088 patent.

43. Defendants’ commercial manufacture, use, offer to sell, or sale of the Actavis ANDA Product within the United States, or importation of the Actavis ANDA Product into the United States, during the term of the ’088 patent also would infringe the ’088 patent under 35 U.S.C. § 271(a), (b), (c), (f) and/or (g).

44. Defendants’ commercial manufacture, use, offer to sell, or sale of the Actavis ANDA Product within the United States, or importation of the Actavis ANDA Product into the United States, during the term of the ’088 patent, would infringe at least Claim 1 of the ’088 patent because, CyDex is informed and believes, and thereon alleges, that the Actavis ANDA Product contains a sulfoalkyl ether cyclodextrin (SAE-CD) composition that can be readily mixed with an active agent, comprising a sulfoalkyl ether cyclodextrin having an average degree of substitution of 4.5 to 7.5 and less than 200 ppm of a phosphate, wherein the SAE-CD composition has an absorption of less than 0.5 A.U. due to a UV-active impurity as determined by UV/vis spectrophotometry at a wavelength of 245 nm to 270 nm for an aqueous solution containing 300 mg of the SAE-CD composition per mL of solution in a cell having a 1 cm path length.

45. Teva’s Purported Notice Letter does not identify any non-infringement argument based on a contention that any claim limitation of any claim of the ’088 patent is not satisfied by the Actavis ANDA Product.

46. Upon approval of the Actavis ANDA, and the commercial marketing of the Actavis ANDA Product, Defendants would actively induce and/or contribute to infringement of the ’088 patent.

47. CyDex is informed and believes, and thereon alleges, that, at least in light of the prescribing instructions Defendants propose to provide in connection with the Actavis ANDA Product, Defendants will induce health care professionals, resellers, pharmacies, and end users of the Actavis ANDA Product to directly infringe one or more claims of the ’088 patent. CyDex is informed and believes, and thereon alleges, that Defendants will encourage acts of direct infringement with knowledge of the ’088 patent and knowledge that they are encouraging infringement.

48. CyDex is informed and believes, and thereon alleges, that Defendants had actual and constructive knowledge of the ’088 patent prior to filing the Actavis ANDA, and were aware that the filing of the Actavis ANDA with the request for FDA approval before the expiration of the ’088 patent would constitute an act of infringement of the ’088 patent.

49. Defendants have no reasonable basis for asserting that the commercial manufacture, use, sale, offer for sale, or importation of the Actavis ANDA Product will not contribute to the infringement and/or induce the infringement of the ’088 patent.

COUNT III FOR INFRINGEMENT OF U.S. PATENT NO. 9,493,582

50. CyDex realleges and incorporates by reference the allegations of paragraphs 1-49 of this Complaint as if fully set forth herein.

51. Defendants infringed the ’582 patent, pursuant to 35 U.S.C. § 271(e)(2)(A), by submitting the Actavis ANDA, which seeks approval from the FDA to engage in the commercial

manufacture, use, offer to sell, sale or importation of the Actavis ANDA Product prior to the expiration of the ’582 patent.

52. Defendants’ commercial manufacture, use, offer to sell, or sale of the Actavis ANDA Product within the United States, or importation of the Actavis ANDA Product into the United States, during the term of the ’582 patent also would infringe the ’582 patent under 35 U.S.C. § 271(a), (b), (c), (f) and/or (g).

53. Defendants’ commercial manufacture, use, offer to sell, or sale of the Actavis ANDA Product within the United States, or importation of the Actavis ANDA Product into the United States, during the term of the ’582 patent, would infringe at least Claim 27 of the ’582 patent because, CyDex is informed and believes, and thereon alleges, that the Actavis ANDA Product contains an alkylated cyclodextrin composition, comprising: an alkylated cyclodextrin having an average degree of substitution of 2 to 9; less than 500 ppm of a phosphate; and 0.07% (w/w) or less of a chloride; wherein the alkylated cyclodextrin composition has an absorption of less than 1 A.U., as determined by UV/vis spectrophotometry at a wavelength of 245 nm to 270 nm for an aqueous solution containing 300 mg of the alkylated cyclodextrin composition per mL of solution in a cell having a 1 cm path length.

54. Teva’s Purported Notice Letter does not identify any non-infringement argument based on a contention that any claim limitation of any claim of the ’582 patent is not satisfied by the Actavis ANDA Product or the process by which the Actavis ANDA Product is manufactured.

55. Upon approval of the Actavis ANDA, and the commercial marketing of the Actavis ANDA Product, Defendants would actively induce and/or contribute to infringement of the ’582 patent.

56. CyDex is informed and believes, and thereon alleges, that, at least in light of the prescribing instructions Defendants propose to provide in connection with the Actavis ANDA Product, Defendants will induce health care professionals, resellers, pharmacies, and end users of the Actavis ANDA Product to directly infringe one or more claims of the ’582 patent. CyDex is informed and believes, and thereon alleges, that Defendants will encourage acts of direct infringement with knowledge of the ’582 patent and knowledge that they are encouraging infringement.

57. CyDex is informed and believes, and thereon alleges, that Defendants had actual and constructive knowledge of the ’582 patent prior to filing the Actavis ANDA, and were aware that the filing of the Actavis ANDA with the request for FDA approval before the expiration of the ’582 patent would constitute an act of infringement of the ’582 patent.

58. Defendants have no reasonable basis for asserting that the commercial manufacture, use, sale, offer for sale, or importation of the Actavis ANDA Product will not contribute to the infringement and/or induce the infringement of the ’582 patent.

EXCEPTIONAL CASE

59. This case is exceptional, and CyDex is entitled to an award of attorneys’ fees under 35 U.S.C. § 285.

INJUNCTIVE RELIEF

60. CyDex will be irreparably harmed if Defendants are not enjoined from infringing, and from actively inducing or contributing to the infringement of, the patents-in-suit.

61. CyDex has no adequate remedy at law.

PRAYER FOR RELIEF

WHEREFORE, CyDex prays for a judgment in its favor and against Defendants, and respectfully requests the following relief:

A. A judgment that Defendants have infringed one or more claims of the ’077 patent under 35 U.S.C. § 271(e)(2) by submitting the Actavis ANDA to the FDA;

B. A judgment that Defendants have infringed one or more claims of the ’088 patent under 35 U.S.C. § 271(e)(2) by submitting the Actavis ANDA to the FDA;

C. A judgment that Defendants have infringed one or more claims of the ’582 patent under 35 U.S.C. § 271(e)(2) by submitting the Actavis ANDA to the FDA;

D. A declaratory judgment that, under one or more of 35 U.S.C. §§ 271(a), (b), (c), (f) and/or (g), Defendants’ commercial manufacture, use, offer for sale, or sale in, or importation into, the United States of the Actavis ANDA Product, or inducing or contributing to such conduct, would constitute infringement of one or more claims of the ’077 patent;

E. A declaratory judgment that under one or more of 35 U.S.C. §§ 271(a), (b), (c), (f) and/or (g), Defendants’ commercial manufacture, use, offer for sale, or sale in, or importation into, the United States of the Actavis ANDA Product, or inducing or contributing to such conduct, would constitute infringement of one or more claims of the ’088 patent;

F. A declaratory judgment that under one or more of 35 U.S.C. §§ 271(a), (b), (c), (f) and/or (g), Defendants’ commercial manufacture, use, offer for sale, or sale in, or importation into, the United States of the Actavis ANDA Product, or inducing or contributing to such conduct, would constitute infringement of one or more claims of the ’582 patent;

G. A permanent injunction, pursuant to 35 U.S.C. § 271(e)(4)(B), enjoining Defendants, their affiliates and subsidiaries, and all persons and entities acting in concert with

Defendants from commercially manufacturing, using, offering for sale, selling, or importing into the United States the Actavis ANDA Product within the United States, or importing the Actavis ANDA Product into the United States, until the expiration of the ’077, ’088, and ’582 patents.

H. An order, pursuant to 35 U.S.C. § 271(e)(4)(A), that the effective date of any FDA approval of ANDA No. 209323 shall be no earlier than the last expiration date of any of the ’077, ’088, and ’582 patents, or the expiration date of any exclusivity to which CyDex is or becomes entitled;

I. An award of damages or other relief, pursuant to 35 U.S.C. § 271(e)(4)(C), if Defendants engage in the commercial manufacture, use, offer for sale, sale, and/or importation of the Actavis ANDA Product, or any product that infringes the ’077 patent, or induces or contributes to such conduct, prior to the expiration of the ’077 patent;

J. An award of damages or other relief, pursuant to 35 U.S.C. § 271(e)(4)(C), if Defendants engage in the commercial manufacture, use, offer for sale, sale, and/or importation of the Actavis ANDA Product, or any product that infringes the ’088 patent, or induces or contributes to such conduct, prior to the expiration of the ’088 patent;

K. An award of damages or other relief, pursuant to 35 U.S.C. § 271(e)(4)(C), if Defendants engage in the commercial manufacture, use, offer for sale, sale, and/or importation of the Actavis ANDA Product, or any product that infringes the ’582 patent, or induces or contributes to such conduct, prior to the expiration of the ’582 patent;

L. A judgment that this is an exceptional case under 35 U.S.C. § 285, and awarding CyDex its reasonable attorneys’ fees;

M. An award to CyDex of its costs and expenses in this action; and

N. Such other and further relief as the Court deems just and proper.

MORRIS, NICHOLS, ARSHT & TUNNELL LLP

/s/ Jack B. Blumenfeld

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